

INSOMNIA AND SOMNOLENCE INDUCED BY SECOND GENERATION ANTIDEPRESSANTS DURING THE TREATMENT OF MAJOR DEPRESSION: A Meta-Analysis

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BACKGROUND

Insomnia and somnolence are side effects frequently associated with second-generation antidepressants and they have been found to reduce both quality of life and compliance with treatment [1]. Despite this evidence, relatively little attention has been given so far to define a clear rank of these side effects across different compounds.

THE AIM OF THE PRESENT META-ANALYSIS IS TO PROVIDE QUANTITATIVE DATA ABOUT SHORT-TERM RATES OF INSOMNIA AND SOMNOLENCE ASSOCIATED WITH COMMONLY EMPLOYED SECOND-GENERATION ANTIDEPRESSANTS DURING THE TREATMENT OF MAJOR DEPRESSION

METHODS

Literature research was conducted using MEDLINE, ISI Web of Science, the Cochrane database and references of retrieved articles. Unpublished documents were provided by pharmaceutical companies and Medical Control Agencies. Included studies had to: 1) focus on patients aged 18 or older; 2) suffering from Major depression (MD) according to the DSM-IV TR criteria; 3) investigate one or more of the above mentioned antidepressants; 4) provide dichotomous measures of drug-related insomnia and/or somnolence rates within the 12th week of treatment; 5) have a minimum duration of six weeks. According to these criteria, 276 studies could be included.

Analysis. Eligible studies were entered in the Cochrane Collaboration Review Manager Software and analyzed by RevMan analysis 1.01. For studies that did not include a placebo control group, we calculated the weighted mean of the placebo samples for the considered variable from placebo-controlled studies that investigated the same variable and applied it to studies not including a placebo group [2]

Sensitivity analyses focused on :

- 1) double-blind, randomized placebo-controlled studies,
- 2) antidepressants mono-therapy studies;
- 3) non-sponsored studies.

RESULTS

Insomnia and somnolence rates in the short-term treatment of MD are shown in **figure 1a and 1b**.

-within 12 weeks, high rates of insomnia were significantly associated to treatment with Bupropion and Desvenlafaxine

- at the opposite, high rates of somnolence were associated to the treatment with Fluvoxamine and Mirtazapine

By sensitivity analysis, slight influences on main findings were observed; however, the results of the general analysis were largely confirmed.

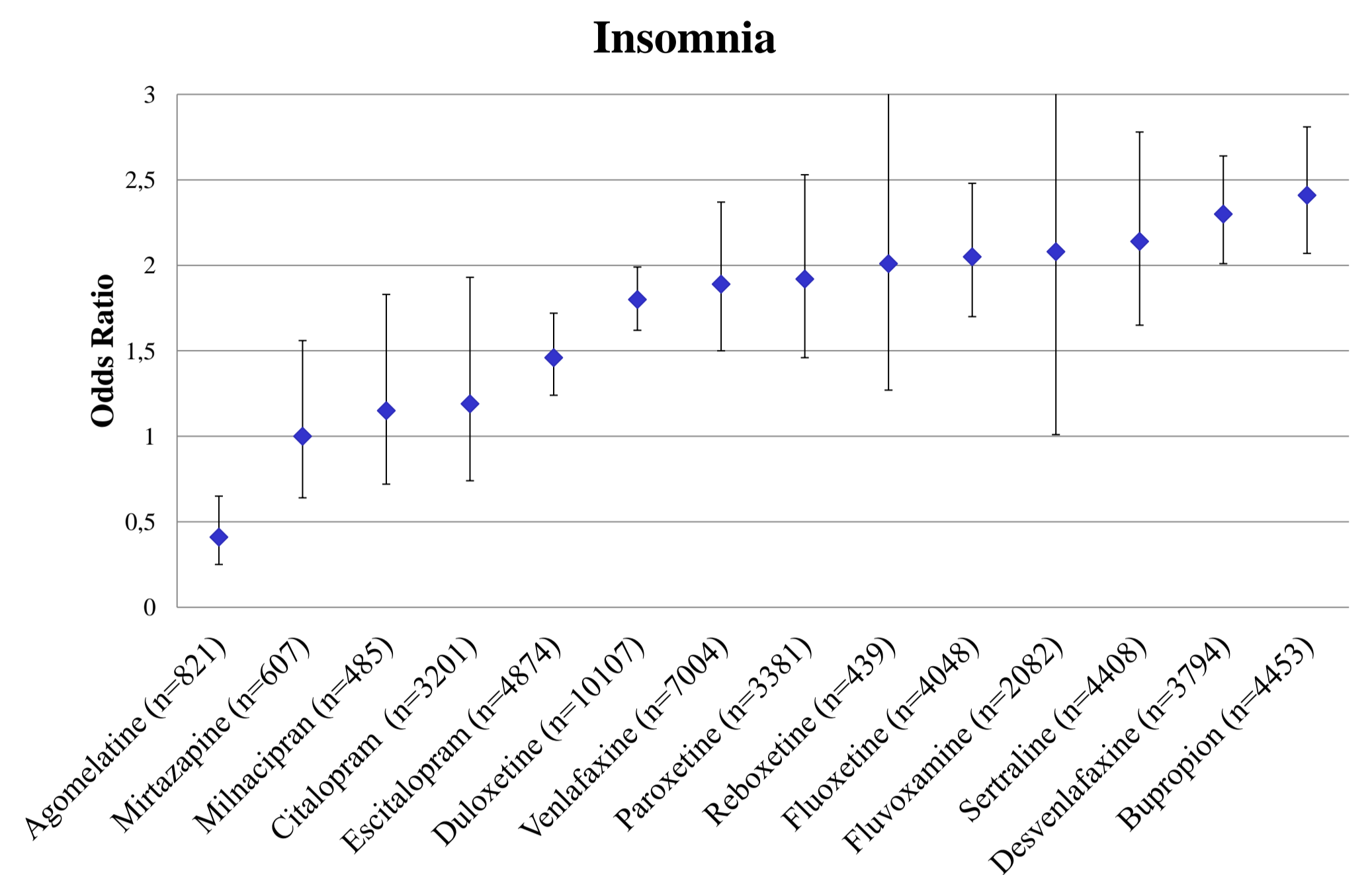


Figure 1a) Insomnia induced by new generation antidepressants as compared to placebo

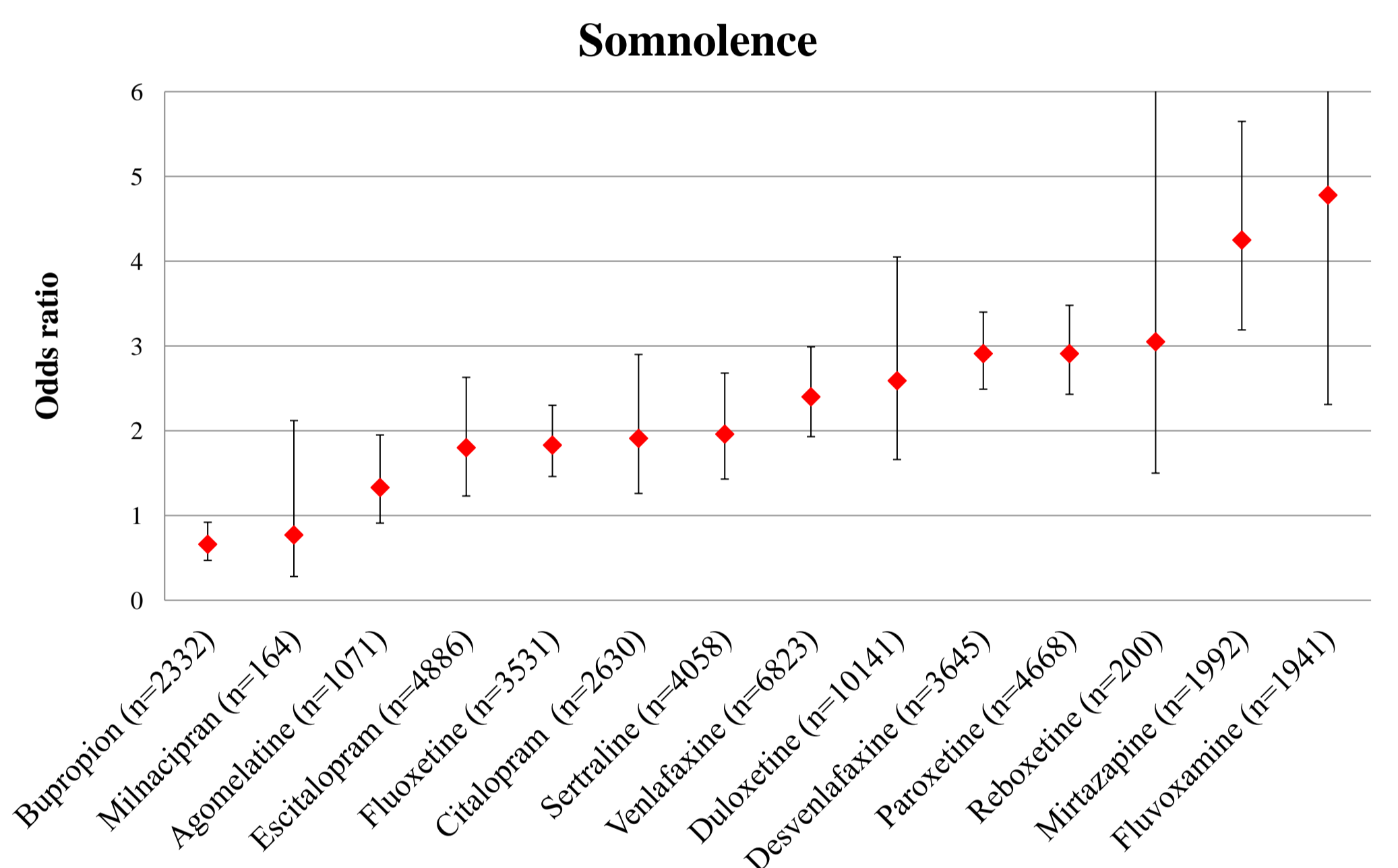
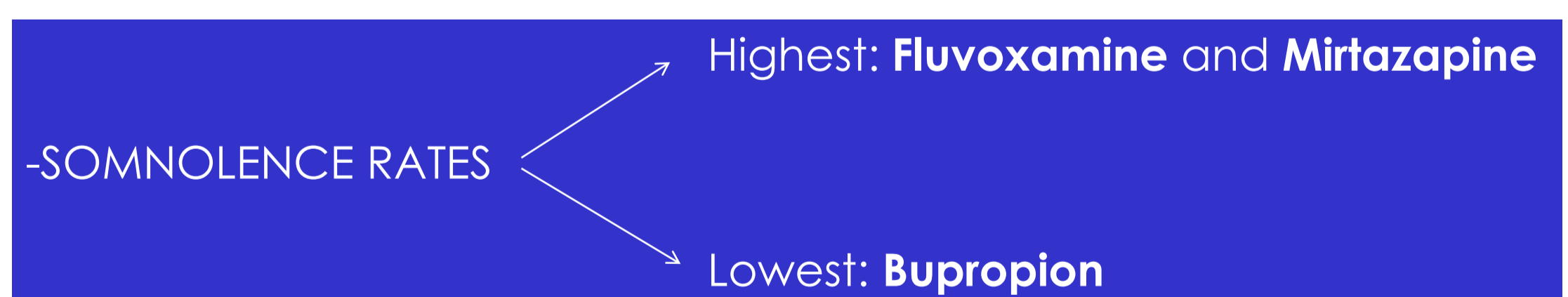


Figure 1b) Somnolence induced by new generation antidepressants as compared to placebo



DISCUSSION

Different antidepressants are associated with different insomnia and somnolence rates; in particular Bupropion, Desvenlafaxine, Agomelatine, Fluvoxamine and Mirtazapine showed the most significant results. These findings are mainly related to their mechanisms of action.

Treatment-related insomnia and/or somnolence are frequent adverse effects that should be considered in clinical practice to best tailor each antidepressant to the specific needs of each patient.

POTENTIAL CONFLICTS OF INTEREST: Dr. Serretti is or has been consultant/speaker for: Abbott, Angelini, Astra Zeneca, Clinical Data, Boehringer, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Innovapharma, Italfarmaco, Janssen, Lundbeck, Pfizer, Sanofi, Servier. Dr. Chiesa is or has been consultant/speaker for: Abbott, Innovapharma. Dr. Andrisano and Dr. Alberti have no conflict to disclose.

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